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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,506	01/05/2005	Heinz Von Der Kammer	P67785US1	6896

136 7590 10/12/2007

JACOBSON HOLMAN PLLC
400 SEVENTH STREET N.W.
SUITE 600
WASHINGTON, DC 20004

EXAMINER	
SHEN, WU CHENG WINSTON	
ART UNIT	**PAPER NUMBER**
1632	

MAIL DATE	DELIVERY MODE
10/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,506	VON DER KAMMER ET AL.	
	Examiner	Art Unit	
	Wu-Cheng Winston Shen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 16-23* is/are pending in the application.

4a) Of the above claim(s) *1-13,16-21 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response received on 07/27/2007 has been entered. Claims 14 and 15 were cancelled. Claims 22 and 23 are newly added. Claims 1-13 and 16-23 are pending.

This application 10/510,506 filed on Jan. 05, 2005 is a 371 of PCT/EP03/03626 filed on 04/08/2003 claims benefit of the provisional application 60/370,214 filed on 04/08/2002.

Election/Restriction

1. The Examiner notes that Applicant's election with traverse of Group VIII, claim 14 (in part), drawn to a protein based assay for screening or testing for a modulator or a compound of neurodegenerative disease, in particular Alzheimer's disease, or related diseases or disorders of a substance of a translation product or a fragment or derivative of the translation product of a gene coding for a vault protein, the minor vault protein ADPRTL1, or a compound for inhibition of binding between a ligand and ADPRTL1 vault protein, in the reply filed on Nov. 15, 2006 was acknowledged.

Newly submitted claim 23 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The newly added claim 23 filed on 07/27/2007 is directed to a transcription product of a gene coding for minor vault protein ADPRTL1 (SEQ ID No: 2), therefore, claim 23 belongs to the subject matter of Group IX of the Restriction Requirement mailed on 09/19/2006 (See bridging paragraph pages 3-4). In this regard, Applicant remark on lines 12-13, page 13 regarding "New claim 23 contains the subject matter of new claim 22, using a different written format" filed on 07/27/2007, is incorrect.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 23 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Accordingly, Claims 1-13, 16-21, and 23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim 22 is currently under examination.

Claim Objections

2. Previous objection of claim 14 because of the following informalities: Recitation of non-elected subject matters: (i) ADPRTL1 gene and (ii) transcription product of ADPRTL1 gene, is ***withdrawn*** because claim 14 has been canceled.

Claim Rejection - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

3. Previous rejections of claim 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is ***withdrawn*** because claim 14 has been canceled.

Claim Rejection - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Previous rejection of claim 14 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is ***withdrawn*** because claim 14 has been canceled.

However, newly added claim 22 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This rejection is necessitated by claim amendments filed by Applicant on 07/27/2007, which added new claim 22.*

For clarity of this office action, Applicant's remark (lines 6-12, page 13) on the newly added claim 22 is cited as follows:

New claim 22 corresponds to previously examined claim 14, amended by limiting the neurodegenerative disease to "Alzheimer's disease, or related diseases or disorders," by reciting (emphasis added) "whereby the modulator is modulating substances selected from the group consisting of," by limiting the Markush group of "substances" to the elected "translation product of a gene coding for a vault protein, the minor vault protein ADPRTL 1 ...and/or... derivatives thereof," and by clarifying that "ADPRTLI" has the amino acid sequence "as shown in SEQ ID

NO: 2." ADPRTL1 corresponds to SEQ ID NO: 2, as disclosed in the subject application (page 11, second paragraph).

Accordingly, claim 22 is directed to an assay for screening for a modulator of Alzheimer's disease, or related diseases or disorders, whereby the modulator is modulating substance selected from *a* translation product of *a* gene coding for *a* vault protein, the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2, and/or ii) derivatives thereof.

With regard to the phrase "derivatives thereof", the phrase encompasses any fragment, or derivative, or variant of a translation product of a gene coding for the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2. In this regard, the specification indicates that the "Proteins and polypeptides" of the instant invention include variants, fragments and chemical derivatives of the protein comprising the amino acid sequence of SEQ ID NO. 2. As indicated in the specification, they can include proteins and polypeptides, which can be isolated from nature or be produced by recombinant and/or synthetic means. Native proteins or polypeptides refer to naturally occurring truncated or secreted forms, naturally occurring variant forms (e.g. splice-variants) and naturally occurring allelic variants (See paragraph [0054], right column, page 3, US 2006/0073480). Relevant to the claimed invention, the specification further discloses that the instant invention further features a protein molecule shown in SEQ ID NO. 2, said protein molecule being a translation product of the gene coding for a vault protein, in particular the minor vault protein ADPRTL1, or a fragment, or derivative, or variant thereof, for use as a screening target for reagents or compounds preventing, or treating, or ameliorating a neurodegenerative disease, preferably Alzheimer's disease (See paragraph [0055], page 8, US 2006/0073480).

With regard to the connection between ADPRTL1 as shown in SEQ ID No: 2 and Alzheimer's disease (AD), the specification discloses that the identification of the differential expression of the human gene coding for minor vault protein ADPRTL1 by a fluorescence differential display screen. The differential expression reflects an *up-regulation of human minor vault protein ADPRTL1 gene transcription* in the temporal cortex compared to the frontal cortex of AD patients (See paragraph [0061], right column, page 9, US 2006/0073480).

It is noted that claim 22 as written would read on any variation (including functionally homologous vault proteins) and/or fragment of the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2. However, the translation products of the genes coding for derivatives of the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2 encompassed within the genus of a gene coding for a vault protein, the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2, and/or derivatives thereof, have not been disclosed. Based upon the prior art there is expected to be variation among the species of genes coding for vault proteins, because the sequence of the genes involved in coding for a vault protein would be expected to vary among individuals. The specification discloses amino acid sequences of human minor vault protein ADPRTL1 as SEQ ID NO: 2 (full length being 1724 amino acid residues). There is no evidence on the record of a relationship between the structure of any vault protein sequences and derivatives thereof, and the claimed SEQ ID NO: 2 sequences for other genes encoding vault proteins that would provide any reliable information about the structure of other vault proteins, variants, and fragments thereof, within the genus. There is no evidence on the record that the asserted human minor vault protein ADPRTL1 sequences had a known structural relationship to any other vault protein sequences; the specification discloses only human minor vault protein ADPRTL1 as SEQ ID

NO: 2 obtained from an undisclosed origin; the art indicated that there is variation between minor vault protein ADPRTL1 (as well as between other vault proteins) and their functions. The specification did disclose the nucleic acid sequences of the gene encoding the human minor vault protein ADPRTL1 as shown in SEQ ID No: 2, the claimed human minor vault protein ADPRTL1, neither did the specification disclose any information regarding the functions of human minor vault protein ADPRTL1 relevant to modulation of Alzheimer's disease, as recited in the claim.

There is no evidence of record that would indicate that any of the claimed variants and fragments of human minor vault protein ADPRTL1 disclosed in SEQ ID No: 2 that share high homology to human minor vault protein ADPRTL1 disclosed in SEQ ID No: 2 even have the biological activity of a minor vault protein ADPRTL1. In the absence of *a functional assay* it would not be possible to test variants of the claimed sequences for biological activity. Also with regard to the claimed allelic variants, the skilled artisan cannot envision the structure of such a variant because such variants are randomly produced in nature, and cannot be predicted from a known sequence. The specification does not teach any characteristics of an "allelic" variant that would distinguish it from a non-natural variant constructed by the hand of man. In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus, because the human minor vault protein ADPRTL1 disclosed in SEQ ID No: 2 is not representative of the claimed genus. Consequently, since Applicant was in possession of only the human minor vault protein ADPRTL1 disclosed in SEQ ID No: 2 and since the art recognized variation among the species of the genus of a vault protein, variants, and fragments thereof, the human minor vault

protein ADPRTL1 disclosed in SEQ ID No: 2 was not representative of the claimed genus. Therefore, Applicant was not in possession of the genus of the genus of a vault protein, variants, and fragments thereof as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

5. Claim 22 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an assay for screening for *a modulator of the minor vault protein ADPRTL1*, whereby the modulator is modulating substances *consisting of* a translation product of a gene coding for a vault protein, the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2, and the method comprising: a) contacting a cell with a test compound; b) measuring the activity and/or level of the substances recited; c) measuring the activity and/or level of the substances in a control cell not contacted with the test compound; and d) comparing the levels and/or activities of the substances in the cells of steps b) and c), wherein an alteration in the activity and/or level of substances in the contacted cells indicates that the test compound is a modulator of Alzheimer's disease, or related diseases or disorders, **does not** reasonably provide enablement for (1) the said assay for screening for a modulator of the minor vault protein ADPRTL1, whereby the modulator is modulating substances being *derivatives of* a translation product of a gene coding for a vault protein, the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2, or (2) the said assay for screening for a modulator of *Alzheimer's disease, or related diseases or disorders*. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. *This rejection is necessitated by claim amendments filed by Applicant on 07/27/2007, which added new claim 22.*

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The nature of the instant invention is directed to an assay for screening for a modulator of the minor vault protein ADPRTL1, whereby the modulator is modulating substance selected from a translation product of a gene coding for a vault protein, the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2. However, Applicant fails to provide a necessary nexus between "a modulator of the minor vault protein ADPRTL1" and "a modulator of Alzheimer's disease, or related diseases or disorders". The specification merely provides that the mRNA

levels of ADPRTL1 in the cells from patients with Alzheimer's disease are up-regulated compared to control healthy subject.

The breadth of the claim encompasses an assay for screening for a modulator of Alzheimer's disease, or any related diseases or disorders, whereby the modulator is modulating substance selected from a translation product of a gene coding for a vault protein, the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2, and/or ii) derivatives thereof. It is noted that the limitation "Alzheimer's disease, or related diseases or disorders" reads on, at least, all neurodegenerative diseases (more elaboration below, and in 102(b) art rejection).

The specification discloses that the identification of the differential expression of the human gene coding for minor vault protein ADPRTL1 by a fluorescence differential display screen. The differential expression reflects an *up-regulation of human minor vault protein ADPRTL1 gene transcription* in the temporal cortex compared to the frontal cortex of AD patients (See paragraph [0061], right column, page 9, US 2006/0073480). This is the only relevant connection between ADPRTL1 as shown in SEQ ID No: 2 and Alzheimer's disease (AD), disclosed in the specification. It is emphasized that, no guidance, prophetic or otherwise, is provided demonstrating that modulation of ADPRTL1 as shown in SEQ ID No: 2 would result in the treatment of Alzheimer's diseases or any related diseases or disorders. Similarly, no working examples are provided at all, prophetic or otherwise, demonstrating the effectiveness of the claimed assay for screening a modulator of Alzheimer's disease, or related diseases or disorders.

With regard to the phrase "derivatives thereof", as discussed in the preceding rejection of claim 22 under 35 U.S.C. 112, first paragraph, written description, the phrase encompasses any

fragment, or derivative, or variant of a translation product of a gene coding for the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2. As indicated in the specification, ADPRTL1 and derivatives thereof can include proteins and polypeptides, which can be isolated from nature or be produced by recombinant and/or synthetic means. The specification further discloses that the instant invention further features a protein molecule shown in SEQ ID NO. 2, said protein molecule being a translation product of the gene coding for a vault protein, in particular the minor vault protein ADPRTL1, or a fragment, or derivative, or variant thereof, for use as *a screening target* for reagents or compounds preventing, or treating, or ameliorating a neurodegenerative disease, preferably Alzheimer's disease (See paragraph [0055], page 8, US 2006/0073480). However, it is noted that the specification does not teach any characteristics of an "allelic" variant and/or a derivative of the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2, that is functional, especially in the context of modulation of Alzheimer's disease, or related diseases or disorders, and can be used as a target for an assay for screening for a modulator of derivatives of the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2. A skilled person in the art will have to conduct experimentation to identify necessary and sufficient fragment(s) required for the function of the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2 (SEQ ID No: 2 being 1724 amino acid residues total) to make and use of the claimed assay using derivatives of the minor vault protein ADPRTL1 as shown in SEQ ID NO: 2 as the target of claimed assay for screening. This level of experimentation is not considered as routine, but is considered as undue.

In the art, neurodegenerative diseases, encompassed by the limitation "Alzheimer's disease, or related diseases or disorders", represent a genus of chronic degenerative disorders,

each with its own vastly different pathophysiology and etiology. For example, Huntington's disease is an autosomal dominant disorder involving a tri-nucleotide repeat expansion and characterized clinically by progressive cognitive impairment, abnormalities of movement, and neuro-psychiatric symptoms (see **Feigin et al,** Recent advances in Huntington's disease: implications for experimental therapeutics, *Curr Opin Neurol.* 15(4): 483-9, 2002). While the exact mechanisms underlying neuronal death in Huntington's are unknown, it is believed that mitochondrial dysfunction and subsequent excitotoxic injury, oxidative stress and apoptosis are to blame for the observed neuro-degeneration occurring in the striatum and other basal ganglia structures. Thus, there would be no expectation that modulation of ADPRTL1 activity, for example as recited in the instant claim, would be of any benefit whatsoever for the treatment and/or modulation of Huntington's disease.

The art also recognizes that Alzheimer's disease is characterized pathologically by a multitude of anatomical abnormalities such as the presence of amyloid plaques, neurofibrillary tangles, changes in permeability of the blood brain barrier leading to vascular damage, as well as neuro-inflammation and neuro-degeneration. See for example **Small et al.** (Small et al., Cerebral metabolic and cognitive decline in persons at genetic risk for Alzheimer's disease, *Proc Natl Acad Sci U S A.* 97(11): 6037-42, 2000). Applicant fails to provide guidance on the treatment of these other features associated with Alzheimer's disease pathology, which would be encompassed by providing therapy (encompassed by the claim limitation "screening for a modulator of Alzheimer's disease" as recited in claim 22 of instant application) to a patient having AD. Thus, while reducing the expression of ADPRTL1, using the claimed modulating substance identified by the claimed assay for screening modulator of ADPRTL1, would be

temporarily reverse the molecular phenotype of Alzheimer's disease, it would not be expected to necessarily provide long-lasting therapeutic results because *up-regulation of ADPRTL1 is not the cause of Alzheimer's disease, rather the up-regulation of ADPRTL1 is the effect of Alzheimer's disease.* Additionally it is noted that both at the time of filing and now, effective therapy for Alzheimer's has eluded researchers despite knowledge and characterization of a number of proteins that are increased and associated with Alzheimer's pathology. **De Lustig et al.** (De Lustig et al., Peripheral markers and diagnostic criteria in Alzheimer's disease: critical evaluations, *Rev Neurosci.* 5(3): 213-25, 1994) report that there are still no effective therapies for the pathology, and the disease thus follows an inevitable degenerative course. And a more recent review by **Vickers** (Vickers, A vaccine against Alzheimer's disease: developments to date. *Drugs Aging.* 19(7): 487-94, 2002) notes that there is no effective treatment currently available to reverse, slow down or prevent the course of Alzheimer's disease and most other brain diseases and conditions. Thus, the art recognizes unpredictability in the ability to effectively treat neurodegenerative diseases, and Alzheimer's disease in particular. It is, therefore, unpredictable, given the lack of guidance in the specification that modulation of ADPRTL1 would treat Alzheimer's in any way.

Therefore, in view of the breadth of the claims encompassing treatment of a vast genus encompassed by "Alzheimer's disease, or related diseases or disorders", the lack of adequate guidance, data, evidence or working examples supporting a therapeutic effect of the claimed assay for screen, the unpredictability in the art of treatment of neurodegenerative diseases and Alzheimer's disease in particular, and the complex nature of modulation of Alzheimer's disease or related neurodegenerative disease encompassed by the claim of instant invention, one of skill

in the art would find that undue experimentation would be required to practice the claimed invention.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Previous rejection of claim 14 under 35 U.S.C. 102(b) as being anticipated by Rome et al., (Rome et al., PCT/US98/11348, WO 99/62547, listed in the IDS filed by the applicants), is ***withdrawn*** because claim 14 has been canceled.

However, claim 22 is newly rejected under 35 U.S.C. 102(b) as being anticipated by Rome et al., (Rome et al., PCT/US98/11348, WO 99/62547, listed in the IDS filed by the applicants) as evidenced by Lam et al., 2001 (Lam et al., beta-Amyloid efflux mediated by p-glycoprotein. *J Neurochem.* 76(4): 1121-8, 2001). *This rejection is necessitated by claim amendments filed by Applicant on 07/27/2007, which added new claim 22.*

Claim interpretation: It is noted that **(i)** minor vault protein ADPRTL1 is also known as VPARP, PHP5, or p193 (See line 4, second paragraph, page 3 of instant application), and **(ii)** the limitation "Alzheimer's disease, or related diseases or disorders" recited in claim 22 of instant application reads on multidrug-resistant (MDR) cancers, taught by Rome et al., 1999, because (a)

the underlying mechanism for development of MDR cancers is the over-expression of P-glycoprotein, and (b) accumulation of β-amyloid (Aβ) in the brain is the underlying cause of Alzheimer's disease, whereas the P-glycoprotein is an β-amyloid efflux pump, as evidenced by Lam et al., 2001. Therefore, MDR cancers and Alzheimer's disease are related diseases at molecular levels hinged on the activity of P-glycoprotein.

Rome et al. teach purified human minor vault protein p193 or purified biologically active variants thereof, or a combination of purified human minor vault protein p193 and biologically active variants thereof are disclosed. A polynucleotide molecule encoding human minor vault protein p193, or the complementary DNA is also disclosed. Furthermore, Rome et al. teach a method of diagnosing and a method of treating patients with multidrug resistant cancer (See abstract, Rome et al., 1999).

More specifically, Rome et al., teach (i) a high affinity monoclonal antibody (which is encompassed by a test compound recited in the step (a) of claim 22 of instant application), which immuno-reacts with human minor vault protein p193 (claim 22, page 25, Rome et al., 1999), (ii) a method of diagnosing a patient with a multidrug-resistant cancer comprising the steps of (a) providing a sample of tissue or fluid from the patient, (b) determining the level of human minor vault p193 protein, which reads on contacting a cell with antibody against human minor vault protein p193, a control without contacting cell with the antibody against human minor vault protein p193, and comparing the levels human minor vault protein p193 with and without antibody (See lines 7-26, page 3; and claim 27, page 25, Rome et al., 1999).

Furthermore, Rome et al. also teach a method of treating a patient with multidrug-resistant cancer comprising the steps of (a) diagnosing a patient with multidrug-resistant cancer

according the method of diagnosing a patient with a multidrug-resistant cancer as recited in the previous paragraph, and (b) treating the patient comprising administering to the patient at least one anti-sense polynucleotide having affinity for a polynucleotide encoding p193, which reads on contacting a cell with anti-sense polynucleotide having affinity for a polynucleotide encoding p193, a control without anti-sense polynucleotide having affinity for a polynucleotide encoding p193, and comparing the biological activity levels of human minor vault protein p193 with and without anti-sense polynucleotide having affinity for a polynucleotide encoding p193 (See claims 29 and 31, page 26, Rome et al., 1999). The abovementioned steps taught by Rome et al. read on the steps (a)-(d) of claim 22 of instant application.

It is noted that the specification fails to define what is encompassed by the terminology "Alzheimer's related diseases or disorders". At the time of filing of instant application, it is known in the art that accumulation of β-amyloid (Aβ) in the brain is the underlying cause of Alzheimer's disease, and it is also known in the art that the P-glycoprotein is an β-amyloid efflux pump, as evidenced by Lam et al., 2001. Therefore, MDR cancers and Alzheimer's disease are related diseases at molecular levels because the development of either disease involved the activity of P-glycoprotein.

Thus, Rome et al. clearly anticipates claim 22 of instant invention.

Conclusion

7. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent

examiner, Peter Paras, can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Wu-Cheng Winston Shen, Ph. D.
Patent Examiner
Art Unit 1632

/Valarie Bertoglio, Ph.D./
Primary Examiner
AU 1632